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Docket No. 4026-P03249US0	Type a plus sign (+) inside this box +

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TITLE OF THE INVENTION (200 characters max)

METHODS OF USING MENTHOL PROPYLENEGLYCOL-CARBONATE AND ANALOGS THEREOF FOR PRODUCING INSECT REPELLENT, ANTI-INFLAMMATORY AND ANTI-ANGIOGENIC EFFECTS

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ENCLOSED APPLICATION PARTS (check all that apply)

X Specification Number of Pages 20

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___ Drawings(s) Number of Sheets _____ Other (specify) Abstract

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Respectfully submitted

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☐ Additional inventors are being named on separately numbered sheets attached hereto

METHODS OF USING MENTHOL PROPYLENEGLYCOL-CARBONATE AND ANALOGS THEREOF FOR PRODUCING INSECT REPELLENT, ANTI-INFLAMMATORY AND ANTI-ANGIOGENIC EFFECTS

Jonathan R. Matias

Background of the Invention

The present invention relates to biological and medical uses of menthol propyleneglycol-carbonate and analogs thereof.

Menthol is a natural product which is obtainable from peppermint oil and other mint oils. Menthol and various analogs thereof, such as (-)-isopulegol, N-ethyl-p-menthane-3-carboxyamide and p-methane-3,8 diol, are used in commerce as cooling agents. These compounds impart a cooling sensation to a variety of products, for example, cosmetics, perfumes, personal care products, oral hygiene products, confectionary, cigarettes, cough drops, nasal inhalants and the like. See, also U.S. Patent No. 5,703,123 to Pelzer, et al.

Menthol has also been applied as a topical antipruitic, and in veterinary medicine as a mild local anesthetic and antiseptic, as well as an internal carminative and gastric sedative. See also, U.S. Patent No. 5,124,320 to Ivy et al.

Menthol and various of its analogs have also been found to possess anti-fouling activity. See published International Patent Application No. PCT/01/40929.

Menthol has been disclosed as one of several components of a miticide in JP 4305505A, and as the essential constituent of a cockroach repellent in JP 55104202A.

Certain analogs and derivatives of menthol have also been disclosed as effective repellents against noxious insects,

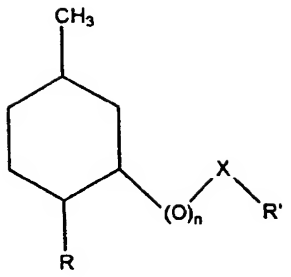
such as mosquitoes, ticks and mites. These include p-menthane-3,8-diol, as described in U.S. Patent No. 5,959,161 to Akiyama et al., and the menthyl ester of pyrrolidone-5-carboxylic acid, as described in U.S. Patent No. 6,451,884 to Watkins et al.

Research into the use of naturally-occurring chemical compounds for applications as insect repellents and topical medications has been motivated, at least in part, by a growing public concern over the possible health risks associated with products of this type that contain synthetic active agents. Consequently, efforts continue toward the development of safe and effective biological and medical agents based on natural compounds.

Summary of the Invention

It has now been discovered, in accordance with the present invention, that carbonic acid derivatives of menthol and various analogs thereof are very effective insect repellents and exhibit anti-inflammatory and anti-angiogenic activity, as well.

This discovery is put to practical advantage in the methods of this invention, in which a carbonic acid derivative of menthol or an analog thereof, as described below, is administered to a mammal in an amount sufficient to produce an insect repellent effect, an anti-inflammatory effect or an anti-angiogenic effect in said mammal. The active agent which produces such effect is a compound of the formula:



(I)

wherein R represents a straight or branched chain, substituted or unsubstituted lower alkyl radical, or a straight or branched chain, substituted or unsubstituted lower alkenyl radical;

X represents a carbonyl linking group (-C(=O)-) or a valence bond;

n is 0 or 1; and

R' represents a radical selected from the group consisting of substituted or unsubstituted hydroxyalkyloxy and substituted or unsubstituted hydroxyalkyl, when n is 1; and R' represents an alkylamine radical when n is 0.

As will appear in the detailed description that follows, compounds of Formula I, above, have utility as repellents against the feeding of insects, particularly mosquitoes, and against crawling insects. Compounds within Formula I are also effective anti-inflammatory and anti-angiogenic agents.

In published International Application PCT/IN02/00228 menthol propyleneglycol-carbonate and menthol ethyleneglycol-

carbonate are disclosed as ingredients of a "cooling cum moisturizing agent" for use as an optional component in an anti-itch formulation. Insofar as is known, however, the compounds described herein as being useful for the practice of this invention have not previously been disclosed or suggested as having insect repellent, anti-inflammatory or anti-angiogenic activities.

Brief Description of the Drawings

Figure 1 is a graphical representation of experimental data showing dose dependent inhibition of mosquito biting by application of a lotion containing various concentrations of racemic menthol propyleneglycol-carbonate.

Figure 2 is a set of photographs showing the degree of angiogenic sprouting inside each of 5 aortic rings at various concentrations of racemic methol propylene glycol-carbonate.

Detailed Description of the Invention

Compounds used in the method of this invention are available from commercial sources, including Symrise GmbH and Takasago International USA, among others. The menthol carbonate derivatives may, if desired, be prepared from readily available starting materials, in the manner described in U.S. Patent No. 5,703,123 to Pelzer, et al. and U.S. Patent No. 3,419,543 to Mold, et al.

The following definitions apply with reference to

compounds encompassed by Formula I, above:

The term "alkyl" refers to straight- or branched-chain unsubstituted alaphatic hydrocarbon groups of 1-12 carbon atoms. Similarly, the term "alkyl", when used in combination form to name a substituent such as "hydroxyalkyloxy", "hydroxyalkyl", "alkylamine" or the like, refers to a straight- or branched-chain alaphatic hydrocarbon group of 1-12 carbon atoms. The expression "lower alkyl" refers to unsubstituted, straight- or branched-chain alkyl groups of 1-6 carbon atoms.

The term "substituted alkyl" refers to an alkyl group substituted by, for example, 1-25 substituents, and most preferably 1-4 substituents. Substituents may include, without limitation, hydroxy, alkoxy, halo, cycloalkoxy, oxo, amino, monoalkylamino, dialkylamino, aryl and substituted aryl. Among the alkyl substituents noted above, particularly preferred are hydroxy substituents.

The term "lower alkenyl" refers to straight- or branched-chain, unsubstituted, unsaturated hydrocarbon groups of 1-6 carbon atoms. Examples of lower alkenyl groups include ethenyl, propenyl, butenyl, pentenyl and the like.

The term "substituted alkenyl" refers to an alkenyl group substituted by, for example, 1-12 substituents, and most preferably, 1-4 substituents. The substituents are the same as those described above with reference to the alkyl groups.

The term "aryl" refers to monocyclic or polycyclic aromatic hydrocarbon groups having 6-15 carbon atoms in the ring

portion, such as phenyl, naphthyl, biphenyl, indenyl, fluorenyl or the like, each of which may be substituted.

The term "substituted aryl" refers to an aryl group, as defined above, substituted by, for example, 1-7 substituents, and preferably, 1-4 substituents, such as those described above with reference to the substituted alkyl and alkenyl groups.

The term "halogen" refers to fluorine, chlorine, bromine or iodine.

When a moiety is described herein as substituted with more than one substituent, it is intended that each of the multiple substituents be chosen independently from among the substituents mentioned above.

Compounds encompassed by Formula I, above, have asymmetric carbon atoms, and therefore, can exist as paired enantiomers, differing in their optical activity. The compounds may be used in enantiomerically pure form, in racemic form or in other mixed forms.

Preferred compounds for use in the methods of this invention include: menthol propyleneglycol-carbonate, isopulegol propyleneglycol-carbonate, menthyl-9-hydroxynonyl-carbonate, menthoxy-propane-1,2-diol, and N-ethyl-p-menthane-3-carboxamide.

In carrying out the methods of the invention, the compounds of Formula I may be used neat, or as a component of a composition obtained by admixture with a suitable carrier or vehicle. The nature of the carrier or vehicle will depend on the end use of the composition, i.e. the effect sought to be

produced, and the mode of administration.

In the case of insect repellent activity, compositions are formulated to include a safe and effective amount of a compound of Formula I which is generally from about 1 to about 80 wt%, based on the total weight of the composition. It has been found that compositions in which a compound of Formula I is present in an amount of less than 1 wt% does not produce the intended effect. The composition may optionally include from about 3 to about 80 wt% of a skin conditioner, with the balance being one or more inactive ingredients that constitute the carrier or vehicle. Particularly satisfactory insect repellent effects have been obtained using formulations containing from about 1 to about 30 wt% of a compound of Formula I above, preferably a racemic mixture of menthol propyleneglycol-carbonate. Isopulegol propyleneglyol-carbonate also produced good results.

The insect repellent effect produced by the compounds described herein may also be incorporated in various cosmetics or personal care products, including, without limitation, perfumes, colognes, deodorants, skin creams, soaps, shampoos, conditioners, hair rinses, bath oils, talcs and the like, or in household products including, without limitation, cleansers, detergents, fabric softeners, air fresheners or the like. These products will typically contain from about 1 to about 80 wt% of a compound or mixture of compounds of Formula I above, based on the tare weight of the product.

The compounds of Formula I can be used as the sole insect repellent in a composition or may be used in combination with other natural or synthetic agents that are effective insect repellents. These include, without limitation, N,N-diethyl-m-toluamide(DEET); N,N-diethylbenzamide; citronella; Tolu balsam; Peru balsam; eucalyptus oil; Huon pine oil; camphor; cypress oil; galbanum; diethylphthalate; dimethylphathalate; dibutylphthalate; 1,2,3a,4,5,5a,6,7,8,9,9a,9b-dodecahydro-3a,6,9a-tetramethylnaphtho[2,1-b]furan; 4-(tricyclo[5.2.1.$0^{2,6}$]decylidene-8)butanal; 1-ethoxy-1(2'-phenylethoxy)ethane; acetyl cedrene and propylidene phthalide.

Compounds of Formula I may also be formulated with a pharmaceutically acceptable carrier material for administration as an anti-inflammatory agent. A safe and effective amount of the active component for this application is from about 1 wt% to about 30 wt% based on the total weight of the formulation. Satisfactory anti-inflammatory effects have been obtained using menthoxy-propane-1,2-diol, racemic menthol propyleneglycol-carbonate, isopulegol propyleneglycol-carbonate and menthyl-9-hydroxynonyl carbonate.

When used in an anti-angiogenic formulation, a safe and effective amount of the compound of Formula I is in the range from about 1 wt% to about 80 wt% based on the total weight of the composition. Satisfactory anti-angiogenic effect has been obtained using racemic menthol propyleneglycol-carbonate.

The specific amount of compound of Formula I to be used

as an anti-inflammatory agent or anti-angiogenic agent may vary depending on differences in potency among the compounds encompassed by Formula I.

In formulations for medical applications, the formulation may contain one or more compounds of Formula I, above, as the active agent, and, optionally, at least one supplemental active agent. The supplemental active agents may include other anti-inflammatory agents, other anti-angiogenic agents, analgesic agents, antibacterial agents, antiviral agents, antifungal agents, antiparasitic agents, tumoricidal or anti-cancer agents, toxins, enzymes, hormones, neurotransmitters, immunoglobulins, immunomodulators, local anesthetics or the like.

Various auxiliary ingredients may be added to the above-described compositions to impart desired properties or characteristics thereto or to facilitate administration in a particular way. These auxiliary ingredients may include, without limitation, fragrances, surfactants, propellants, emulsifiers, dispersants, buffers, preservatives, antioxidants, diluents, solvents, fixatives, pharmaceutical excipients and adjuvants, as is common practice in the art.

The deleterious activity of microorganisms may be inhibited by the inclusion of various antibacterial and antifungal agents, e.g., paraben, chlorobutanol, phenol, sorbic acid and the like.

The compositions described above may be prepared in various forms depending on the mode of administration. Thus,

compositions may be in the form of a lotion, cream, ointment, gel or powder for topical application or a solution or suspension for administration as an atomized or aerosol spray. Alternatively, the composition may, if desired, be in the form of tablets, capsules or microparticulates filled into gelatin capsules, or the like, for oral administration. The composition may also be formed as a suppository for rectal or vaginal administration.

The compounds and compositions described herein may be formulated with sustained release components or carriers of various types, e.g. in alcohol or in water-based formulations for topical use, as is well known in the art.

Compositions used in practicing the invention can be prepared by various methods well known in the art. Typically, such compositions are prepared by intimately mixing a compound of Formula I with a suitable carrier material and optionally one or more supplemental active agents of auxiliary ingredients, as desired, and putting the resulting mixture into a suitable container or dispenser.

The compounds and compositions described herein may be administered systemically or locally, e.g. by application to exposed or inflamed areas of skin or by rectal or vaginal delivery. Topical administration is preferred. The expression "systemic administration" refers to delivery of an active agent such that it enters the recipient's system and thus, is subject to metabolic processes. Systemic administration encompasses both enteral and parenteral administration, the latter including,

without limitation, intravenous, intramuscular, intramedullary, intraperitonal and subcutaneous administration, as well as administration by inhalation.

The compounds and compositions described herein are beneficially administered to mammals, particularly to humans, to produce the desired insect repellent, anti-inflammatory or anti-angiogenic effect.

The following examples set forth further details regarding the invention. These examples are provided for illustrative purposes only, and are not intended to limit the invention in any way. These examples show the results of tests conducted to determine the efficacy of certain compounds of Formula I, above, as insect repellents, anti-inflammatory agents and anti-angiogenic agents.

Examples 1 and 2 show the insect repellent effect of compounds of Formula I, above:

Example 1

Adult mosquitoes (Culex quinquefasciatus) were kept inside a screened chamber measuring 2 ft X 2 ft X 2 ft at a density of 200 mosquitoes per chamber. The mosquitoes are aged 3 to 10 days after emergence from larvae and were starved for 24 hours prior to each test. The test compound was added to a commercial lotion base (Cresto Laboratories, Manila, Philippines) and thoroughly mixed into the lotion using an electronic mixer. The resulting formulation was applied from the elbow to the tip

of the fingers of human volunteers. The coated arms of the volunteers were then inserted, in turn, inside the chamber up to the elbow. The protection time was determined for each formulation as the length of time until a mosquito had taken its first bite, after which the test was terminated. The data in Table 1 show the protection time determined in this manner for the compounds tested.

TABLE I

Chemical Name (Synonym)	Protection Time (minutes)*
1-5-methyl-2-isopropyl cyclohexanol (l-menthol)	60 ± 9
5-methyl-2-(1-methylethenyl) cyclohexanol ((-)-isopulegol)	56 ± 7
menthoxy-propane-1,2-diol	68 ± 17
N-Ethyl-p-menthane-3-carboxyamide	92 ± 31
menthol propyleneglycol-carbonate	68 ± 15
racemic menthol propyleneglycol-carbonate	283 ± 17
isopulegol propyleneglycol-carbonate	152 ± 36
menthyl-9-hydroxynonyl-carbonate	79 ± 14

*Mean ± Standard error of the mean for 4 volunteers per test group. Compounds were added to the lotion base at a concentration of 5 wt%, based on the total weight of the composition.

The data show that the racemic form of menthol propyleneglycol-carbonate is almost five times more effective than menthol or isopulegol in preventing mosquito bites.

Further experiments demonstrated that the inhibitory effect of racemic menthol propyleneglycol-carbonate on mosquito bite

occurs in a dose dependent manner. The results of these experiments are shown in Figure 1.

Example 2

The red ant (pharaoh ant, *Monomorium pharaonis*) was selected for this ant repellent test since it has a worldwide distribution and is known to be a household pest.

Red ants are attracted to the smell of food. The attractant in this experiment was a piece of chocolate, which was placed on a tabletop 5 hours before the test. Within 2 hours after being released on the ground around the table, the red ants established a route from the ground up the table legs. At the 5th hour, a filter paper impregnated with racemic menthol propyleneglycol-carbonate at two concentrations was placed around the middle portion of the table leg. The test compound was dissolved in ethanol and added to a pre-weighed, 2 inch by 7 inch piece of filter paper. After complete evaporation of ethanol, the filter paper was weighed and the final weight of the test compound was determined per cm^2 of the filter paper. The control employed was the same filter paper soaked with ethanol only. The time for the first ant to cross the filter paper barrier was determined.

The data are shown in Table II. The results show that racemic menthol propyleneglycol-carbonate, at appropriate concentration, is an effective repellent against red ants.

TABLE II

TEST GROUP	Concentration (mg/cm^2)	Time to cross barrier * (Minutes)
CONTROL	0	< 1
Menthol propyleneglycol-carbonate (racemic)	15	63 ± 18
Menthol propyleneglycol-carbonate (racemic)	30	760 ± 76

Each data point is the mean ± SEM of 5 tests.

Example 3 shows the anti-inflammatory effect of compounds of Formula I, above.

Example 3

Edema was induced by topical application of 10μl of TPA(Tetradecnoylphorbol acetate) in acetone (2.5μg/ear) to both the inner and outer surface of one ear of each mouse used in the experiment. Each test compound, diluted with acetone to a concentration of 10-% was applied topically to the inflamed mouse ear immediately after TPA application, so as to deliver 2.5 mg/ear. The reference drug, indomethacin (0.5mg/ear), was administered as a positive control. The thickness of each ear was measured before treatment and 4 hours after induction of inflammation, using a micrometer (Mitutoyo Co.). Anti-inflammatory effect was expressed as the reduction in ear thickness with respect to the control group. The results obtained are presented in Table III.

TABLE III

CHEMICAL NAME	Anti-inflammatory Effect (% of control)
(l)-Menthol	0
menthoxy-propane-1,2-diol	27
N-Ethyl-p-menthane-3-carboxyamide	11
menthol propyleneglycol-carbonate	27
racemic menthol propyleneglycol-carbonate	23
isopulegol propyleneglycol-carbonate	33
menthyl-9-hydroxynonyl-carbonate	45
Indomethacin	96

The data show that all of the compounds of the invention that were tested exhibited substantial inhibition of TPA-induced inflammatory response, in comparison to menthol, which showed no appreciable anti-inflammatory effect under the test conditions employed.

Example 4 shows the anti-angiogenic effect of racemic menthol propyleneglycol-carbonate.

Example 4

The effect of racemic menthol propyleneglycol-carbonate on angiogenesis was studied by culturing aortic explants in three-dimensional matrix gels according to the procedure of Kruger and Figg (Kruger E.A. and Figg, W.D. Protein Binding Alters the Activity of Suramin, Carboxyamidotriazole, and UCN-01 in an *ex Vivo* Rat Aortic Ring Angiogenesis Assay Clinical Cancer

Research 7:1867-1872, 2001).

Thoracic aortas were excised from 8-week-old mail Sprague Dawley rats and the fibroadipose tissue was removed. The aortas were sectioned into 1-mm-long cross-sections, rinsed with Human Endothelial-SFM(GIBCO), placed on the Matrigel-coated wells, covered with additional 50 μl Matrigel, and allowed to gel for more than 30 min at 37ºC, 5% CO_2. All the rings were cultured in Human Endothelial-SFM(GIBCO) supplemented with 200μl/ml of ECGS(Endothelial Cell Growth Supplement, Sigma) as an angiogenesis inducer. Racemic menthol propylene-carbonate diluted with enthanol was added to the culture medium at final concentrations of 1, 10, and 100μM. Ethanol alone (1%) was added to the culture medium as a vehicle control.

All assays were performed by using 5 aortic rings per sample. Aortic rings were photographed on day 10. These photographs are shown in Figure 2. The area of angiogenic sprouting was calculated using Image-Pro Plus software (Media Cybernetics). The image analysis quantitation of the dose-response activity of racemic menthol propyleneglycol-carbonate is shown in Table IV. Microvessel densities are reported in square pixels.

TABLE IV

Concentration (uM)	Microvessel Density (pixel^2)	% Inhibition
0	15.8 ± 4.0	0
1	13.4 ± 4.1	15
10	12.2 ± 2.5	22
100	10.6 ± 3.8	33

The data indicate that racemic menthol propylene-carbonate inhibited microvessel formation in rat aortic ring assay in a dose dependent manner.

Example 5 describes the results of a cell cytotoxicty assay performed to evaluate the ctytoxic effect of racemic menthol propyleneglycol-carbonate on normal cells.

Example 5

5 X 10^3 Ha-CaT cells were plated in each well of 96 well plates and racemic menthol propyleneglycol-carbonate was added at various concentrations. The plates were incubated for another 48 hours and the viable cells were measured by XTT Cell Proliferation Kit (Roche). More than 70% of Ha-CaT cells were viable even at high concentration of 100μM. The results of this experiment are shown in Table V.

TABLE V

Concentration (uM)	Cell Viability (%)
0.1	100
1.0	100
5.0	96.5
10.0	96.3
50.0	81.8
100	70.4

These data show that racemic menthol propyleneglycol-carbonate is non-toxic against normal cells.

Example 6 shows the results of an experiment conducted to determine the effect of racemic menthol propyleneglycol carbonate on HUVE cell proliferation.

Example 6

HUVE (Human Umbilical Vein Endothelial) cells were isolated from human umbilical cord veins by a method of Jaffe et al. (Jaffe, E. A., Nachman, R. L., Becker, C. G., and Minick, C. R. Culture of Human endothelial cells derived from umbilical veins. J. Clin. Invest. 52: 2745-2756, 1973). HUVE cells were confirmed by immunostaining with antibody against factor VIII. The cells were grown in M199 medium(Gibco BRL, Grand Island, NY) supplemented with 10% fetal bovine serum, 100units/mL penicillin, 100μg/mL streptomycin, 50 μg/mL endothelial cell growth supplement, and 5 units /mL heparin at 37 °C in an atmosphere of 5% CO_2-95% air.

1 x10^4 HUVE cells were plated in each well of 96 well plates and five different concentrations ranging from 1 to 100 of racemic menthol propyleneglycol-carbonate were tested in the presence of bFGF used as maximum proliferation control. Cells were cultured for an additional 48 hours, and relative cell numbers in each well were determined by XTT Cell Proliferation Kit (Roche).

The results are presented in Table VI.

	No bFGF	bFGF only	MPC-r* 100μM	MPC-r 50μM	MPC-r 10μM	MPC-r 5μM	MPC-r 1μM
Average	0.2283	1.0830	0.9121	1.0621	1.0425	1.0305	1.0623
Proliferation(%)	0.0	100.0	80.0	97.6	95.3	93.9	97.6

* MPC-r = racemic menthol propyleneglycol-carbonate

As can be seen from the data in Table VI, 100 uM of menthol propyleneglycol-carbonate weakly inhibited HUVE cell proliferation by 20%. The results show that this compound does not have detrimental effects on the normal proliferation of endothelial cells.

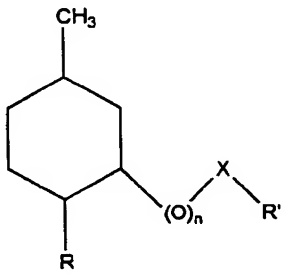
The data set forth in the foregoing examples indicate that compounds of Formula I, above, are: (1) effective as insect repellents; (2) effective as anti-inflammatory agents when applied topically; and (3) effective as anti-angiogenesis agents.

While certain embodiments of the present invention have been described and/or exemplified above, various other

embodiments will be apparent to those skilled in the art from the foregoing disclosure. The present invention is, therefore, not limited to the particular embodiments described and/or exemplified, but is capable of considerable variation and modification without departure from the scope of the appended claims.

What is claimed is:

1. A method for achieving an effect in a mammal, wherein the effect is an insect repellant effect, an anti-inflammatory effect or an anti-angiogenic effect, said method comprising administering to said mammal, in an amount sufficient to produce said effect, a compound of the formula:



wherein R represents a straight or branched chain, substituted or unsubstituted lower alkyl radical, or a straight or branched chain, substituted or unsubstituted lower alkenyl radical;

X represents a carbonyl linking group (-C(=O)-) or a valence bond;

n is 0 or 1; and

R' represents a radical selected from the group consisting of substituted or unsubstituted hydroxyalkyloxy and substituted or unsubstituted hydroxyalkyl, when n is 1; and R' represents an alkylamine radical when n is 0.

2. The method of claim 1 wherein the compound of Formula I

is administered in the form of a composition, also including a suitable carrier, the amount of said compound being from about 1 wt% to about 50 wt% based on the total weight of said composition.

3. The method of claim 2, wherein the amount of said compound is from about 1 wt% to about 80 wt%, based on the total weight of said composition.

4. The method of claim 1, wherein the compound of Formula I is administered to produce an insect repellant effect.

5. The method of claim 4, wherein the compound of Formula I is selected from the group consisting of menthol propyleneglycol-carbonate and isopulegol propyleneglycol-carbonate, said compound being in enantiomerically pure form or in racemic form.

6. The method of claim 4, wherein the compound of Formula I is racemic menthol propyleneglycol-carbonate.

7. The method of claim 4, wherein the compound of Formula I is isopulegol propyleneglycol-carbonate.

8. The method of claim 1, wherein the compound of Formula I is administered to produce an anti-inflammatory effect.

9. The method of claim 8, wherein the compound of Formula I is selected from the group consisting of menthoxy-propane-1,2-diol, N-ethyl-p-menthane-3-carboxyamide, menthol propyleneglycol-carbonate, isopulegol propyleneglycol-carbonate and menthyl-9-hydroxynonyl carbonate, said compound being in an enantiomerically pure form or in racemic form.

10. The method of claim 8, wherein the compound of Formula I is menthoxy-propane-1,2-diol.

11. The method of claim 8, wherein the compound of Formula I is racemic menthol propyleneglycol-carbonate.

12. The method of claim 8, wherein the compound of Formula I is isopulegol propyleneglycol-carbonate.

13. The method of claim 8, wherein the compound of Formula I is menthyl-9-hydroxynonyl carbonate.

14. The method of claim 1, wherein the compound of Formula I is administered to produce an anti-angiogenic effect.

15. The method of claim 14, wherein the compound of Formula I is racemic menthol propyleneglycol-carbonate.

16. The method of claim 1 wherein the compound of Formula I is administered by topical application to said mammal.

17. The method of claim 16, wherein said compound is administered as a sustained release formulation.

18. The method of claim 1, wherein the compound of Formula I is administered for achieving said effect in a human.

Abstract of the Disclosure

Menthol propyleneglycal-carbonate, analogs thereof and compositions containing such compounds are administered to mammals, preferably humans, to produce insect repellent, anti-inflammatory and anti-angiogenic effects.

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